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BUMED NEWS LETTER

a digest of timely information

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Plague: Epidemiology: Plague is primarily a disease of a large number of species of wild and domestic rodents. In rodents the disease may be either acute or chronic, either epizootic or enzootic. When it occurs in wild rodents,

it is usually known as sylvatic plague. Plague in humans is usually contracted through the bites of infected fleas, although infection may occur in other ways. The causative bacterium is Pasteurella pestis, a gram-negative, pleomorphic, bipolar bacillus. Three clinically and epidemiologically distinct types of human plague occur: bubonic, pneumonic and septicemic.

Geographic distribution: It is difficult to describe accurately the geographic distribution of plague. A careful examination of rodent population throughout the world would be required to ascertain reliably the distribution of plague. The geographic distribution of plague is continually changing and is intimately associated not only with the dispersal of plague through rodent populations but also with the migrations of the rodents themselves. Because the common commensal rats often are infected, plague can be spread in addition by the transportation of these rats in trains, airplanes and ships. Since the pandemic of 1894-1900 epidemic plague has decreased considerably in incidence. At the present time the heavy foci of human plague exist in Manchuria, parts of China, Indo-China, Java, Burma, India, British East Africa, Morocco and Madagascar. Small epidemics and sporadic cases have been reported in U.S.S.R., Spain, France, Senegal, Nigeria, New Caledonia, Belgian Congo, Angola, Algeria, Tunisia, Egypt, Union of South Africa, Ecuador, Peru, Bolivia, Chile, Argentina, Brazil, Iraq, Lebanon, Thailand, and Hawaii. Foci of sylvatic plague are known to exist in western United States, Hawaii, Manchuria, Mongolia, China, Lake Baikal region of U.S.S.R., South Africa, British East Africa, Morocco, Madagascar, Venezuela, Colombia, Peru, Bolivia, Argentine, Paraguay, Brazil and the Guianas.

Vectors: Xenopsylla cheopis (Rothschild), the Oriental rat flea, is the most important rodent-to-man plague vector. This species has a wide distribution in eastern Asia and as far north as the Amur River country, in Japan Formosa, Philippine Islands, Malay Archipelago, Malaya, Burma, India, Ceylon, Australia, numerous areas in Africa (including Madagascar), southern Europe and the Near East, the United States except the area between the Mississippi River and the Rocky Mountains and in numerous areas in South America and the West Indies. It is primarily a parasite of rats and mice. Xenopsylla astia (Rothschild), which occurs on rats and mice in India, Burma, Ceylon, Mesopotamia and Java, is a rather inefficient and occasional rat-to-man vector. Other rodent-to-man vectors are Xenopsylla brasiliense (Baker) (India and Africa), Xenopsylla nubicus (Rothschild) which replaces cheopis in Africa, possibly Ctenocephalides canis (Curtis) (cosmopolitan), and Nosopsyllus fasciatus (Bosc) (originally European - now cosmopolitan in and near harbor cities). Pulex irritans L. may serve as a man-to-man vector when it becomes infected from biting human septicemic cases. The above-mentioned fleas, with the exception of Pulex irritans, are important also as rodent-to-rodent vectors. Among others known to serve as rodent-to-rodent vectors are Xenopsylla eridos (Rothschild) (southern Africa) Ctenopsyllus

segnis (Schoenherr) (cosmopolitan on house mice), Xenopsylla hirsuta (Rothschild) (southern Africa), and Dinopsyllus lypusus (Jordan and Rothschild) (Africa). Many other species of fleas in various parts of the world are doubtlessly involved in rodent-to-rodent transmission of plague.

There are several important points concerning the infection of fleas with plague which should be emphasized. In the first place a relatively small percentage of those which feed on infected animals actually become infected. Furthermore, infected fleas do not become infective unless the esophagus is blocked by a bacterial mass. Such fleas are unable to suck blood, and after becoming hungry become restless and bite voraciously. These are the individuals that transmit plague. "Blocked" fleas rarely survive more than 48 hours after the development of the block. Although both sexes may transmit the disease, females are more efficient than males. Plague infection usually causes fleas to die. In the case of Xenopsylla cheopis death occurs within a month after infection; Nosopsyllus fasciatus may survive for from two to four months. Feces of infected fleas contain plague bacilli which, when deposited on the skin, may gain entrance to the body through scratches.

Fleas have only general host specificity. Xenopsylla cheopis, for instance, is primarily a rodent flea, although it also attacks man and predatory mammals. In plague epizootics, when large numbers of domestic rats die, these fleas attack man readily. This is an important point in the epidemiology of plague.

Reservoir hosts: Many species of rodents are known to be susceptible to plague; it seems possible that all rodents can be infected. Among the domestic species known to serve as reservoirs and immediate sources of infected fleas in epidemics of bubonic plague are the domestic species such as Rattus norvegicus (Berkenhout), the Norway rat; Rattus rattus rattus (L.), the black rat; Rattus rattus alexandrinus (E. Geoffroy), the roof rat; Rattus rattus diardii (Jentink), the Malayan house rat; and possibly Rattus rattus rufescens (Gray), the common Indian rat. The first three are world-wide in their distribution and are associated with trade and commerce, whereas rufescens and diardii are Oriental in their distribution. All are readily transported from area to area by man. Rattus rattus frugivorus (Rafinesque) should also be included in this group. These species are frequently affected by epizootics of plague and under such circumstances are the immediate sources of infected fleas in bubonic epidemics.

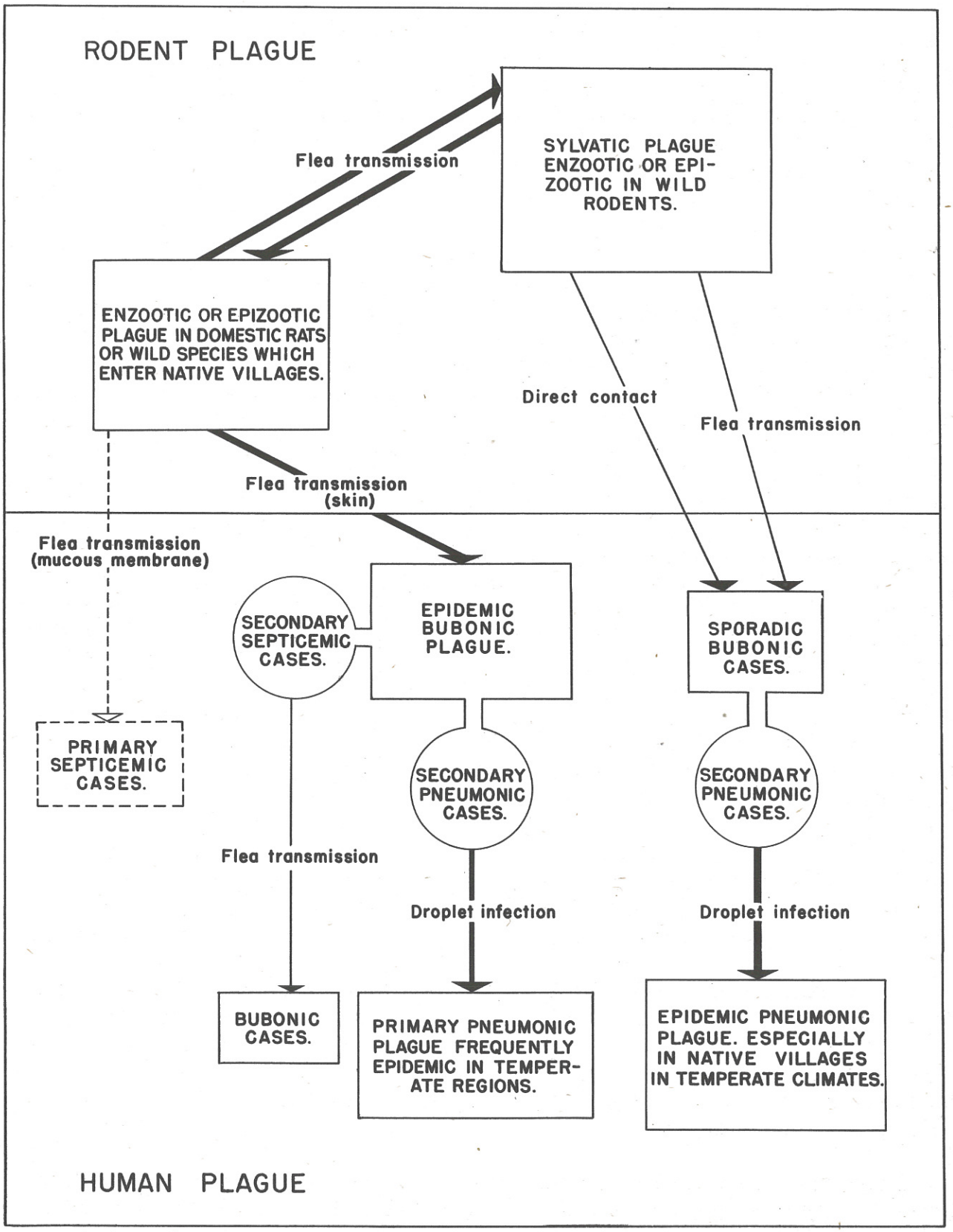
Certain other species, although not domestic in habit, are frequently in contact with native populations and are of importance. In Java, for instance, Rattus rattus argentiventer (Robinson and Kloss), Rattus rattus roquei Sody,

Rattus concolor ephippium (Jentink) and Rattus concolor otteni Kopstein have such habits.

The true sylvatic reservoirs are usually rodents of the families Sciuridae (squirrels, ground squirrels, susliks, etc.) and Gerbillinae (gerbils). This has been found to be true in enzootic areas of sylvatic plague in Mongolia, Manchuria, Astrakhan, South Africa and (?) South America. They constitute a vast uncontrollable reservoir from which domestic rats may become infected and from which sporadic human bubonic cases are derived. In Java wild species of rats serve as reservoirs. Rodents of the families Muridae (rats and mice), Jaculidae (jumping rats) and Leporidae (rabbits and hares) are complementary plague hosts. Certain rodents which are primarily wild species are probably important in plague transmission because of the fact that they occasionally enter dwellings and in so doing spread the infection to the domestic species. Examples are Microtus arvalis, which in Astrakhan enters human dwellings in the fall and in which plague occurs epizootically, and Rattus coucha which in South Africa is affected epizootically and which may come in contact with the domestic rats.

Epidemiology and control: The epidemiology of plague is extremely complex. The plague potentiality of an area is affected by the proximity of sylvatic reservoirs and the habits of the species involved, the species and population densities of the domestic rats present, the flea fauna of the reservoirs and domestic rats, the relation of the human population to the rat population, climate, importation of rats from other areas, housing, density of human population and numerous other factors. With the exception of epidemics in certain native populations, large plague epidemics almost invariably arise as the result of epizootics in populations of domestic rats. When the rate of infected domestic rats rises to five per cent or more, there is cause for alarm and immediate control measures are indicated. When these rats die, their fleas, particularly Xenopsylla cheopis, attack humans, resulting in the development of bubonic cases. Bubonic cases may become pneumonic secondarily and from these, especially in temperate areas, primary pneumonic cases develop. These relationships of human and rodent plague are outlined in the Table. Although bubonic or pneumonic cases may become septicemic, it is probably only rarely that fleas become infected by attacking man. Among crowded natives in temperate regions epidemics of pneumonic plague develop from a few secondary pneumonic cases which were originally sporadic bubonic cases derived from sylvatic reservoirs.

The primary principles in plague prevention are preventing immigration of rats into the area involved and controlling the rat population within it, since these species constitute the immediate source of infected fleas. When rat control is practiced during plague epidemics, special precaution must be taken against attacks by fleas from dead rats. In addition, prophylactic immunization should be carried out.


RODENT PLAGUE
Flea transmission
SYLVATIC PLAGUE ENZOOTIC OR EPI-ZOOTIC IN WILD RODENTS.
ENZOOTIC OR EPIZOOTIC PLAGUE IN DOMESTIC RATS OR WILD SPECIES WHICH ENTER NATIVE VILLAGES.
Direct contact
Flea transmission
Flea transmission (skin)
Flea transmission (mucous membrane)
SECONDARY SEPTICEMIC CASES.
EPIDEMIC BUBONIC PLAGUE.
SPORADIC BUBONIC CASES.
PRIMARY SEPTICEMIC CASES.
SECONDARY PNEUMONIC CASES.
SECONDARY PNEUMONIC CASES.
Flea transmission
Droplet infection
Droplet infection
BUBONIC CASES.
PRIMARY PNEUMONIC PLAGUE FREQUENTLY EPIDEMIC IN TEMPER-ATE REGIONS.
EPIDEMIC PNEUMONIC PLAGUE. ESPECIALLY IN NATIVE VILLAGES IN TEMPERATE CLIMATES.
HUMAN PLAGUE

The above measures are those directed against plague epidemics. Prevention of sporadic cases derived from sylvatic plague is difficult unless enzootic areas can be avoided. Control of the wild-rodent plague reservoirs is impracticable. In both epidemic and sporadic cases of plague strict isolation should be enforced, and one should bear in mind the fact that the plague bacillus may persist in the convalescent patients as long as three weeks after all symptoms have disappeared. (Prev. Med. Div., BuMed - D. S. Farner)

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Plague: Preventive Medicine and Therapy: A formalin-killed plague vaccine is available on the Supply Table (S1-180). This vaccine has not been tested in large series of cases with respect to the incidence of plague in vaccinated individuals and unvaccinated controls. However, its experimental injection into animals is followed by the development of a considerable degree of immunity. In some instances its use in man has been followed by moderately severe local and general reactions. Recently collected reports on approximately 5,500 antiplague vaccinations in the Armed Forces and in 7,500 civilians indicate that this vaccine may produce local as well as general reactions in a small, though variable, percentage of persons inoculated. The local reactions occasionally lead to abscess formation (Meyer OEMcmr-259). According to a report recently received by the Bureau, out of one group of 9,781 naval personnel vaccinated, five had reactions severe enough to necessitate rest in bed for 24 hours (Gezon).

The vaccine should be administered to naval personnel prior to their entry into areas where plague is endemic as well as to personnel upon the occasion of an outbreak of plague in the vicinity of the place in which they are stationed.

Vaccines consisting of suspensions of living avirulent plague bacilli have been used frequently, especially in North Africa, Madagascar and Java. Because of the possibility of their transmitting the disease through being inadequately attenuated, their employment in naval personnel is not recommended.

The treatment of plague with sulfonamides was discussed in the Bumed News Letter of March 3, 1944. Reports of the effectiveness of these drugs vary in different series because of differences in the technic of administration as well as because of the great difference in the threat to life presented on the one hand by bubonic plague and on the other by the pneumonic and septicemic forms of the disease.

There appears to be little room for doubt that sulfonamides are effective in the therapy of plague, especially the bubonic form. All workers emphasize the fact that sulfonamides to be effective must be given early in the course

of the disease and for at least twelve days after the return of the temperature to normal. Treatment should begin with heavy dosage. Sulfadiazine is the drug of choice. It is considerably more effective than sulfathiazole in the therapy of experimental Pasteurella pestis infections in animals.

A recent report to the Bureau concerning a small epidemic of bubonic plague occurring in a native population reveals some interesting facts with respect to treatment. There were 19 cases in the series. Five victims were found dead or were admitted to the hospital in a moribund condition and died a few hours after admission. Two patients were treated only with 80 c.c. of antiplague serum over a period of two days. Both seemed to be making dramatic recoveries, but after being allowed up on the fourth day, they suddenly died. Death was said to have been due to myocarditis. The other ten patients, who were seen early in the course of the disease, received treatment with sulfadiazine in heavy dosage at the onset followed by a lower dosage for a considerable period of time. Seven of these ten patients received, in addition, 50 c.c. of antiplague serum. All ten recovered (Gezon).

Plague, especially in its pneumonic form, is highly communicable, and medical department personnel caring for patients with this disease should be afforded the benefit of all available means of protection. The strictest isolation technic should be maintained. Protective vaccination must be carried out. It is recommended that prophylactic doses of sulfadiazine (at least 2.0 Gm. a day) be given.

Sheep antiplague sera have been widely used in the treatment of plague. Their effectiveness has not been demonstrated. Efforts to obtain a potent serum through immunization of horses have not been successful. At present no antiplague serum of proved value is available in this country. Meyer has recently developed a rabbit serum which offers promise. The best therapeutic results in experimental P. pestis infections in guinea pigs were obtained when both rabbit serum and sulfadiazine were used.

Penicillin has no bacteriostatic activity against P. pestis in vitro, and it has failed therapeutically in laboratory infections. It is therefore not anticipated that penicillin will be effective in the treatment of plague.

Streptomycin and streptothricin (mentioned elsewhere in this issue) have been found to possess bacteriostatic action in vitro in high dilution against plague bacilli and have proved effective (Meyer) in the treatment of experimental plague in animals. (Prev. Med. Div., BuMed - J. K. Curtis; Prof. Div., BuMed - F. A. Butler)

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Streptomycin and Streptothricin: New Antibiotics: The search for a chemotherapeutic agent effective against infections due to gram-negative organisms recently led to the isolation by Waksman and Woodruff (1) of streptothricin, derived from Actinomyces lavendulae. More recently a second antibiotic substance, streptomycin, has been isolated by Schatz, Bugie and Waksman (2) in crude form from a microorganism called Actinomyces griseus.

According to Waksman and his co-workers (3), these substances deserve careful consideration as promising therapeutic agents. Both streptothricin and streptomycin are characterized by selective bacteriostatic activity against gram-positive and gram-negative bacteria. They are similar in their activity in vivo. Streptomycin has much greater activity against certain specific gram-positive and certain gram-negative bacteria than does streptothricin. Bacillus mycoides, Serratia marcescens and the human strain of Mycobacterium tuberculosis, for example, are sensitive to streptomycin and fairly resistant to streptothricin, whereas Staphylococcus aureus, Bacillus subtilis and Escherichia coli are sensitive alike to both substances. Both compounds are highly stabile.

Both substances possess limited toxicity for animals. According to Robinson (4) the nature of the toxic effects produced by streptomycin and streptothricin appears to be identical, and these effects appear to be due to a histamine-like substance present in the more toxic preparations. Robinson believes that streptomycin possesses certain advantages over streptothricin from the standpoint of toxicity.

The greater action of streptomycin as compared with streptothricin against certain gram-negative and gram-positive bacteria makes the former appear from the therapeutic standpoint also to be the more valuable drug.

In experiments using animals both drugs have been shown to be active in vitro against a variety of bacteria, streptomycin being more effective against specific organisms, such as Pseudomonas aeruginosa and Proteus vulgaris.

Numerous other experiments in vivo have been carried out with highly favorable results. It is sufficient to mention, in this connection, the results obtained in experiments with mice and chick embryos infected with Salmonella aertrycke, Salmonella schottmulleri or Brucella abortus and treated with streptothricin, and those infected with Salmonella schottmulleri, Pseudomonas aeruginosa, Shigella gallinarum or Brucella abortus and treated with streptomycin.

The need for a chemotherapeutic agent effective against gram-negative bacilli is great, and streptomycin gives promise of fulfilling it. Extensive

toxicological and pharmacological studies of streptomycin will, however, have to be completed before the value of this substance in the treatment of bacterial disease in animals and man can be finally determined.

(1) S.A. Waksman & H.B. Woodruff, Proc. Soc. Exper. Biol. & Med., Oct. '40.
(2) A. Schatz, E. Bugie & S.A. Waksman, Proc. Soc. Exper. Biol. & Med., Jan. '44.
(3) S.A. Waksman, E. Bugie & A. Schatz, Proc. Staff Meet., Mayo Clin., Nov. 15, '44.
(4) H.J. Robinson, D.G. Smith & O.E. Graessle, Proc. Soc. Exper. Biol. & Med., Nov. '4

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Gramicidin S: A strain of Bacillus brevis isolated from Russian soil has been investigated in detail, and a crystalline product of high antibacterial activity, named Gramicidin S, has been prepared from the sediment obtained after the acidification of fluid cultures. This substance, which has the properties of a polypeptide, may be compared with gramicidin and tyrocidine, the crystalline polypeptides with antibacterial properties which Dubos and Hotchkiss prepared from cultures of another strain of B. brevis. Like tyrocidine, but unlike the gramicidin of Dubos, gramicidin S acts in high dilutions against both gram-positive and gram-negative bacteria. It differs from tyrocidine in retaining its activity against gram-negative bacteria in nutrient broth. No evidence is given whether, like tyrocidine, it is inhibited by blood and serum. Since none of these substances is soluble in water, there is no question of systemic use in therapeutics. Both of the substances of Dubos are, however, of low toxicity to tissue cells relative to their antibacterial power, and gramicidin and the crude product tyrothricin, which contains both gramicidin and tyrocidine, have been used locally in medical and veterinary practice in the United States with some success. From the brief report of a clinical trial of gramicidin S in a wide variety of local infections the results appear to be promising. (Lancet (Annotations) - Dec. 9, '44.)

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Physiological Effects of Salicylates: The segregation at the U.S. Naval Hospital, Corona, Calif., of naval personnel who have developed rheumatic fever has provided the staff of that activity with an unusual opportunity to study this disease and reappraise some of the presently used methods of therapy. A number of investigations are being conducted. Through the courtesy of Captain Leake and the members of the Rheumatic Fever Service, the Bumed News Letter will be permitted from time to time to present in brief form the results of some of these investigations prior to the appearance of the papers in standard medical publications.

Some of the studies are concerned with the action and effects of salicylate as it is administered in the treatment of rheumatic fever. A renewed

interest in salicylate therapy was aroused slightly more than a year ago by a paper of Coburn which was presented in abstract form in the Bumed News Letter of November 12, 1943. In this paper Coburn reported that when the plasma level of salicylate could be maintained at 35 or more mg. per c.c., patients in the early acute phase of rheumatic fever responded promptly with clinical improvement, return of the elevated sedimentation rate to normal levels and disappearance of clinical signs of myocarditis. The response in a group of controls treated with smaller doses was much less striking.

Coburn and Kapp had shown in previous immunological studies that salicylate prevented the precipitation of an antigen by its antibody in vitro, that this effect became more marked as the concentration of salicylate in the solution was increased, and that the immune system became progressively less sensitive to the action of salicylate as the excess of antibody became larger (more salicylate being required to offset antibody excess). Coburn naturally suggested the possibility that the plasma salicylate concentrations achieved by the higher dosage schedules which he recommended might inactivate in vivo the reaction between the antibody formed by the rheumatic subject and the antigen produced by the hemolytic streptococcus.

So convincing was the evidence as to the greater effectiveness of the higher dosage schedule advised by Coburn that it was recommended by the Bureau that it be adopted in the treatment of rheumatic fever in the Navy.

Patients in the early phase of acute rheumatic fever are not available for study at Corona. Therefore, the original investigation of Coburn could not be repeated. However, the staff at Corona has had an excellent opportunity to observe the action of high dosage of salicylates in the later phases of the disease and to study the physiological and pharmacological effects of salicylates in general.

The effect of salicylate on the prothrombin level: Salicylic acid was found in 1943 by Link to be a chemical degradation product of 3,3'-methylene-bis-(4-hydroxy-coumarin), the substance found in spoiled sweet clover which inhibits the synthesis of prothrombin. Link demonstrated that following injection into rats of salicylic acid there occurred a temporary fall in the level of prothrombin which could be prevented or reversed by the administration of adequate amounts of vitamin K. Since then these observations have been confirmed by other investigators. The question naturally has been asked whether the maintenance of high blood levels of salicylate might result in an increase in the prothrombin time sufficient to produce hemorrhagic manifestations clinically. The situation is further complicated by the fact that hemorrhagic tendencies are part of the clinical and pathological picture of rheumatic fever.

The group at Corona measured in 51 subjects the effect on the prothrombin content of the blood of sodium salicylate administered over a relatively long period of time. The daily dosage of sodium salicylate and sodium bicarbonate administered to the subjects and the daily dosage of sodium bicarbonate administered to controls were as follows:

	SUBJECTS		CONTROLS
	Sodium Salicylate	Sodium Bicarbonate	Sodium Bicarbonate
1st Week	3.30 Gm.	1.2 Gm.	1.2 Gm.
2nd "	6.75 Gm.	2.4 Gm.	2.4 Gm.
3rd "	10.00 Gm.	4.0 Gm.	4.0 Gm.
4th "	12.00 Gm.	4.0 Gm.	4.0 Gm.

The changes in prothrombin levels in the men to whom sodium salicylate was administered are of considerable interest. During the first week (daily dosage 3.3 Gm.) no changes occurred. In the second week, however, two days after the dosage had been increased to 6.75 Gm. the prothrombin time began to increase in a small number of cases. It was not, however, until the third week, when the subjects had been on a dosage of 10 Gm. sodium salicylate for two days, that a good percentage of the subjects had a prolongation of the prothrombin time. However, with even greater increase in the dosage of salicylate (to 12 Gm.) the prothrombin time did not increase further. Prothrombin determinations in the controls showed no appreciable change in level during the four weeks that they received sodium bicarbonate. At no time during this study were any abnormal hemorrhagic manifestations noted in the 51 subjects taking salicylates.

In the course of the study of the 105 patients used in this investigation, it was observed that some of them were not taking their medication properly. This fact was easily determined by following the blood salicylate levels of these patients. In another experiment in which the primary purpose was to determine the effect of sodium bicarbonate on the blood-salicylate level, the prothrombin time was followed. In this group which consisted of nine patients, supervision of medication was extremely strict and all received their prescribed medication. They were given 10 Gm. of sodium salicylate daily for a period of three weeks with and without sodium bicarbonate. The Quick prothrombin time and blood salicylate level were done daily.

As previously noted by other investigators, the prothrombin time did not rise until about the second or third day. In all of these subjects the blood salicylate level was between 30 and 50 mg. per cent throughout the study. In spite of this high salicylate level, there was no significant progressive increase in the number of individuals who had a reduced prothrombin

level. Even at this dosage of salicylate, the increase in prothrombin time was not marked. At no time in any patient was any hemorrhagic manifestation noted during this study.

These observations confirm previous reports that salicylate has some effect on the prothrombin content of the blood. However, they suggest that this effect is minimal, and that with even high dosage of salicylate the prothrombin content of the blood is not dangerously reduced. Hemorrhage from therapeutic administration of salicylates is certainly unlikely. On the other hand, if any surgical procedure is contemplated for a patient with rheumatic fever who is taking large doses of salicylates, vitamin K obviously should be given pre- and postoperatively.

The effect of salicylate on the hepatic parenchyma: The Van den Bergh reaction was indirect before, during and after the study in all of the individuals taking part. Likewise the serum bilirubin was not increased above normal in any instance, nor was hepatic function altered as measured by the dye-retention method. Under the conditions of this experiment, therefore, the salicylates administered even in large doses had no detectable deleterious effect upon the parenchyma of the liver.

Blood salicylate levels: Among those patients in whom it could be verified that the medication was taken as ordered, the blood-salicylate level at a dosage of 10 Gm. a day of sodium salicylate varied between 30 and 50 mg. per cent. After medication had been discontinued, the blood salicylate level fell very rapidly and was nearly zero at the end of three or four days. From this observation it would seem that an adequate blood level of salicylate is maintained in most individuals on an oral dosage of between seven and ten grams of sodium salicylate daily.

The effect of salicylate on the sedimentation rate: It has been shown by Coburn and others that the maintenance of a high level of salicylate in a first acute attack of rheumatic fever is followed by a rather rapid fall in the blood sedimentation rate. In the studies at Corona, it was found that in spite of continuous administration of salicylate there were a few patients who developed polycyclic recurrences of rheumatic fever with subsequent rise in the blood sedimentation rate. Most of these patients had adequate blood salicylate levels. In spite of this continued high dosage of salicylate, the sedimentation rate remained elevated in a few of these subjects throughout the study. Among the controls there was nearly an equal number of rises in the blood sedimentation rate, which in most instances represented a recurrence of rheumatic fever.

These studies suggest that subacute rheumatic fever does not respond clinically, nor does the sedimentation rate respond, to the administration of

salicylates in a manner comparable to that observed in a first acute attack. At present, there is no known explanation for this interesting difference.

Effect of salicylate on the blood and urine: While long continued high dosage of salicylates was found to be followed by a very slight reduction in the hemoglobin content and the erythrocyte count, it is very likely that this change in the blood picture was due to the disease rather than the drug. The leukocyte count was unaffected in both the subjects and the controls. Among the group of 51 subjects there were only six who in one specimen had a few leukocytes in their urine. Similar observations were noted in eight of the controls. In neither subjects nor controls was albumin noted on any occasion.

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The medical officers participating in this research at Corona were: Lt. Comdr. Hugh R. Butt, (MC), USNR; Capt. William H. Leake, (MC), USNR; Comdr. Robert F. Solley, (MC), USNR; Lt. Comdr. George C. Griffith, (MC), USNR; Lt. Comdr. Robert W. Huntington, (MC), USNR; Lt. Comdr. Hugh Montgomery, (MC), USNR.

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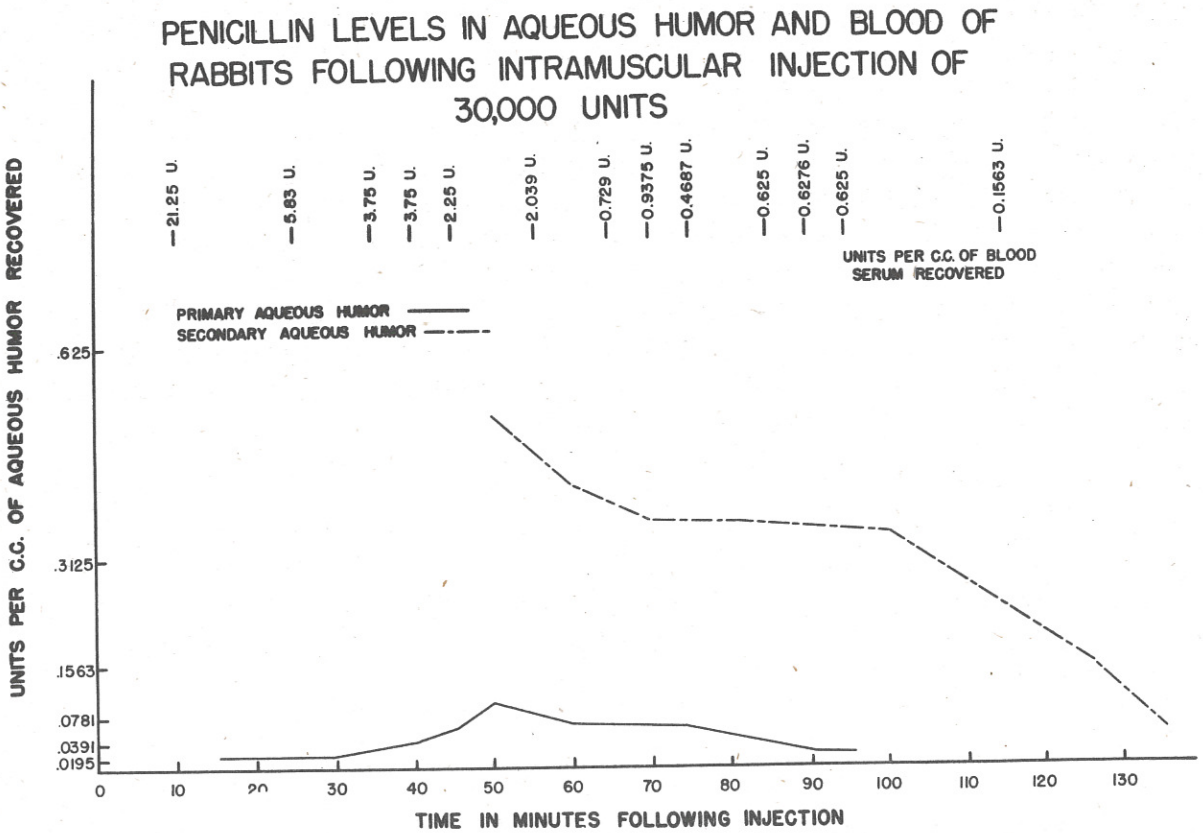
Concentration of Penicillin in the Aqueous Humor Following Parenteral Injection: Studies using rabbits, confirmed by tests in which monkeys were used, have shown that penicillin is present in the aqueous humor following systemic injection. Concentration of the drug is always low in the primary aqueous fluid in spite of high blood levels. Massive doses are required to produce an appreciable increase in this concentration. However, the concentration is considered sufficient to be of clinical value at a dosage of 7,000 units per kilogram of body weight in the rabbit and monkey. Repeated, frequent injections maintain a low level without increment.

Following paracentesis of the anterior chamber, the secondary or plasmoid aqueous reforms within 40 minutes in sufficient quantity to produce normal tension in the anterior chamber. Concentration of penicillin in this fluid is higher than that in the primary aqueous and approaches the level in blood serum collected five minutes prior to the taking of the secondary aqueous sample. It is apparent that, as the intraocular fluid reforms after paracentesis, the penicillin is transmitted directly from the blood as one of the plasma constituents. These findings suggest that an infection accompanying a perforating injury to the eyeball might be expected to respond more readily to parenteral injection of the drug than one in which there is no escape of the intraocular fluid.

The concentration of penicillin in the primary aqueous following a single intramuscular injection gradually increases, with a peak at 50 minutes.



The rate of decrease is slow, a fairly constant level being maintained for at least 90 minutes. The changes in concentration of drug in the secondary aqueous follow, in general, the changes in blood concentration. Although the level in the secondary aqueous is never as high as that found in early blood samples, resorption is slow, with the result that a curve of concentration plotted against time would start at a lower level but would fall more gradually to approach or equal the blood level curve at 100 minutes after a single intramuscular injection of penicillin (See Graph).

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The Control of Experimental Anterior Chamber Infections with Systemic Penicillin Therapy: Experimental studies have shown that a relatively uniform infection of the anterior chamber of the rabbit eye can with regularity be produced for study of the action of antibacterial agents. In the experiments reported here, a penicillin-sensitive streptococcus was used, but equally satisfactory infections have been produced with staphylococcus.

Penicillin by intramuscular injection was found to be effective in controlling and eradicating such experimentally produced infections in the rabbit, provided massive injections were given every three hours over an extended period of time.

In a series of ten experimental animals with induced streptococcal infection of the anterior chamber, therapy with penicillin by intramuscular injection of approximately 5,000 units per kilogram of body weight was started as soon as there was clinical evidence of keratitis. Bacteriological studies revealed the presence of viable bacteria in the aqueous humor of the four animals tested prior to initiation of therapy. Because paracentesis is followed by the formation of a secondary aqueous fluid with a high concentration of the constituents of blood serum and because penicillin is readily transmitted to the aqueous fluid in this manner to produce a higher level than is found in the eye in which paracentesis has not been done, it was deemed wise to refrain from withdrawing the aqueous humor in some of the animals until the infection was shown to be under control by clinical examination. Culture of each of the ten animals was negative for streptococcus by the eighth day. Penicillin therapy was discontinued at this time.

Conjunctivitis, which occurred concurrently with the anterior-chamber infection, subsided rapidly. Hypopyon was present in seven of the ten eyes studied and exudate was observed in the pupillary area in eight. This exudate usually appeared first as a purulent collection which progressed under treatment to a thin membranous exudate attached to the margin of the iris. In every instance, it had completely disappeared by the sixteenth day after therapy was started. It is of interest to note that the opacities, when they occurred, were at the site of needle puncture. The corneas which showed minute areas of opacity had been subjected to multiple puncture. It would appear that perforation of the cornea in the presence of an infection in the anterior chamber leads to a localized infection which is not readily accessible to therapeutic agents. The regimen of therapy for one series of animals included, in addition to systemic injection of penicillin, the withdrawal of aqueous humor twice daily in an effort to increase the concentration of the antibacterial agent at the site of infection. It was demonstrated that this manipulation in the presence of an infection aggravated the condition to such an extent as to outweigh the beneficial effect of higher levels of penicillin. This observation in no way invalidates a previous observation that anterior-chamber infection accompanied by perforating injury can be expected to respond more readily to systemic treatment than a closed infection without loss of aqueous fluid. (Nav. Hosp., Nav. Med. Res. Inst., Bethesda - A. E. Town & F. C. F. Young)

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Local Injection of Penicillin in Treatment of Pneumococcal Empyema: Local injections of penicillin were used to treat 21 cases of pneumococcal empyema. Twenty of the patients recovered without evidence of residual chronic infection, thoracic deformity, or reduction in pulmonary function. In 14 of the patients a single series of one to five injections on alternate

days was followed by recovery. In seven relapse occurred, but six of these responded to reinstitution of local treatment. The only case in which this mode of therapy was unsuccessful was a child of two years, who was operated upon when the early treatment was followed by a relapse.

The empyema fluid was promptly sterilized by penicillin, which by in vitro tests was shown to be active 48 hours after injection. In no case did relapse occur when the empyema fluid was demonstrated to have been sterile for as long as eight days following cessation of treatment.

The clearing of deposits of exudation on the pleural surfaces, as determined by X-ray, required from three to nine weeks. However, the interval between the first and last successful thoracenteses averaged 24 days.

The general health of the patients during the post-therapeutic period of resolution was good. (Tillett et al., New York Univ. - To be published. CMR Bulletin #22.)

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Experimental Transmission of Epidemic Hepatitis: Havens et al have recently carried out an experiment on the transmission of epidemic hepatitis, using 19 volunteers at two institutions. Three different samples of serum containing the hepatitis-producing agent were inoculated intracutaneously into five human subjects, and the disease was produced in three after incubation periods of from 56 to 70 (average 64) days.

Three volunteers were fed (or given intranasally) sera suspected of containing icterogenic agent. Of these, two contracted epidemic hepatitis with severe clinical jaundice 30 days after feeding and the third developed mild subicteric hepatitis after 84 days. Six volunteers were fed urine and stool extracts obtained from patients in various stages of epidemic hepatitis. Of these volunteers, two contracted hepatitis 20 and 22 days respectively following feeding. (Proc. Soc. Exper. Biol. & Med., Nov. '44.)

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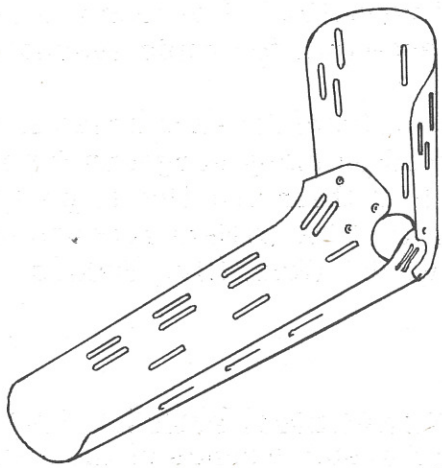
Neurocirculatory Asthenia: Familial Incidence of the Chronic Type: Family histories of 57 patients with the chronic form of neurocirculatory asthenia (from a military hospital in the Zone of the Interior) and of 51 normal soldiers were analyzed in an attempt to determine the incidence of this disorder in parents and siblings. The data indicate that there were definite cases of neurocirculatory asthenia in the families of 65 per cent of the neurocirculatory-asthenia patients and of 1.8 per cent of the controls. (Progress Report #11, OEMcmr-157 - P. D. White, Massachusetts General Hospital. CMR Bulletin #21)

New Type of Plastic Arm Splint Used in Evacuation: A new type of arm splint has been designed which should be useful under combat conditions in which the requirements of rapid evacuation demand prompt immobilization.

The splint is made of a phenolic fabric board which is very light and strong and which is resistant to moisture and to tropical deterioration. It is constructed in two parts: the section for the upper arm is 9-5/16 inches long and that for the forearm is 18-1/2 inches long. The two sections are attached to each other by rivets in such a way as to form a right angle. Both sections are pierced by numerous slots, which provide a means of securing the splint to the arm and of allowing adequate drainage. It is molded and shaped to provide immobilization for any fracture of the arm or forearm. The splint may be applied to either the right or the left arm and is designed to fit an arm or forearm of any size. The construction is such that temporary traction may be applied if it be desired.



The splints are supplied in "nested" stacks of 12. They are expendable and much more easily handled than Thomas arm splints. They may be considered the upper-extremity counterpart of the plywood leg splints which have proved so valuable in this war.

The designers are Capt. F. R. Moore (MC), USN, and Comdr. P. J. O'Donnell (MC), USNR.

As supplies of these splints are received by the Naval Medical Supply Depot, Brooklyn, N. Y., they are being shipped to Advance Base Depots for delivery to combat organizations. (Plan. Div., BuMed - J. Scripp, Jr.)

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Traction vs. Simple Immobilization in Fractures Sustained in Combat: Considerable controversy has arisen over the relative merits under combat conditions of the traction-type temporary splint and the encasement-type non-traction splint.

The Thomas splint is functionally ideal in that it provides immobilization by traction which works toward final reduction. However, under

conditions of battle it has certain disadvantages. It is a cumbersome apparatus, not easily stored or transported. It is not considered expendable. When applied to a patient, it may be difficult to handle. Furthermore, the application of traction to an extremity for a considerable period of time frequently results in ischemia, which may cause discomfort or even gangrene. There may also be painful pressure at the site of counter traction.

Under combat conditions, speed of immobilization is essential, and the encasement-type splint is the more rapidly applied of the two. It does not offer the hazard of distal ischemia, and although it is not intended to provide final reduction, if properly constructed and applied it offers the immobility essential for rapid evacuation.

Reports from forward areas indicate that the encasement-type splint is preferred by many surgeons for immobilization of fractures during combat. It is their practice to postpone attempts to secure satisfactory reduction until the patient reaches facilities behind the front lines prepared for such work. (Res. Div., BuMed - J. S. Thiemeyer)

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Surgery of Heart Wounds: A series of 23 patients who had been operated upon for stab wounds of the heart or of intracardial portions of great vessels has recently been reported by Elkin. This series supplements one of 38 cases reported by the author in November 1940. Practically all of the patients were operated on by members of the resident staff of the Emory University Division of the Grady Hospital, Atlanta, Georgia.

The mortality rate in the earlier series was 42 per cent as compared with a mortality rate in the later series of 22 per cent. The author attributes this improvement in results to several factors, among which are improvement in skill of the resident surgeons and earlier and more accurate diagnosis. While seven deaths in the first series were believed to have resulted from infection (pericarditis, pneumonia or bacteremia), there were no deaths from this cause in the second series. The reduction in mortality from infection was not due to the use of sulfonamides, since in the second series they were used in only one case. In no instance was a sulfonamide placed in the wound. The author attributes the lower incidence of fatal infection in the later series in the main to more meticulous technic and to more careful preoperative preparation. Another factor which Elkin believes to have been of considerable importance was the giving of intravenous fluid prior to operation.(See next item.)

All of the patients in both series were operated upon because there was definite evidence of cardiac tamponade. This diagnosis was based upon the

presence of lowered arterial pressure and increased venous pressure and the presence of a quiet heart as noted on fluoroscopic examination.

Venous pressure readings are not only of value in the diagnosis of tamponade but are of considerable prognostic importance. If the venous pressure is high, that in itself is evidence that the heart is carrying on its functions and that the cardiac output is at least sufficient to produce such pressure. On the other hand, a low or lowered venous pressure in the presence of tamponade is evidence of a failing heart and of a greatly reduced cardiac output.

It was noted that in all patients there was a definite lowering of the arterial pressure and, in 17 of the 23, blood pressure readings could not be recorded. In those patients who recovered there was an immediate rise in arterial pressure following the release of the tamponade.

Some type of general anesthesia in which positive pressure can be used for inflation of the lung is preferable to local anesthesia. The difficulties of heart suture require that the patient be quiet, and patients with wounds of the heart are usually excited or may become so with the release of the tamponade. Unless they are completely anesthetized, their movements may interfere with the operation at the most inopportune time.

The operative approach to the heart is made on the left side of the sternum, with the incision placed about one intercostal space below the external wound. In most instances a transverse incision extending from about two centimeters outside the nipple line and carried well across the sternum has been used. By this approach one or two ribs can be removed, and if necessary the adjacent costal cartilages cut and a portion of the sternum removed. The pectoralis major muscle is separated in the direction of its fibers and can be retracted from the surface of the three ribs. Every care should be taken to prevent opening the pleura, since such a complication adds materially to the shock which the patient has already undergone. The internal mammary vessels must be carefully isolated and ligated. They may not bleed before the tamponade is released, but later hemorrhage from them may be fatal unless proper ligation has been performed. The pleura on the left is displaced from the pericardium by gauze dissection and held out of the wound by a wet pack. As a rule, the pericardium will be tense, and its pulsations weak or imperceptible. If the wound in the pericardium is seen, it should be enlarged or, if it is not readily found, an opening should be made between stay-sutures. Occasionally the heart wound can be located before the blood and clots are removed and before the heart starts beating actively, and under such conditions it can be readily sutured. More often the heart wound is not disclosed until blood and clots are removed by suction. When the intrapericardial pressure is relieved, the bleeding becomes marked and contractions of the heart increase in force. When the wound is located, and it is

most often found in the right ventricle, its closure is facilitated by placing the left index finger over it. In this way the bleeding will be impeded sufficiently to allow the passage of a suture directly under the finger. This is left untied for the moment and is held in the left hand for traction hemostasis while other sutures are placed and tied. Should the wound be behind the sternum or on the posterior surface of the heart, a stay-suture passed through the apex, as advocated by Beck, is of great value. By this means the wound may be rotated into a position favorable for suture. Wounds of the coronary vessels may require ligature but are not necessarily fatal. The pericardium should be closed loosely to allow the escape of pericardial fluid, but the chest wall should be sutured with careful approximation of the anatomic layers.

While operation in these series was carried out as soon as the diagnosis of heart wound with cardiac tamponade was established, Colonel Elkin believes that, in view of the reports from other clinics on this subject, in certain cases some form of conservative treatment may be tried if conditions are not urgent and operation does not seem to be immediately demanded. Bigger, Strieder and Blalock have emphasized the value of aspiration of the pericardium as a preliminary to operation. In some instances it has been found that aspiration alone is the only operative procedure necessary, since some wounds, particularly those which do not penetrate the cavities of the heart, have become sealed, and aspiration of the blood relieving the tamponade is sufficient to bring about a cure. Blalock advocates that, in cases of tamponade in which there is no bleeding into the chest or to the outside, the pericardium be aspirated, but that "all facilities should be available for immediate operation if it becomes necessary." He further states that "if blood reaccumulates rapidly following aspiration, it is agreed that exposure and suture of the heart wound are indicated." The direction of the knife-thrust or a bullet wound is notoriously misleading. The position of the cardiac wound cannot be determined by the wound of entrance, and the symptoms of tamponade are the same no matter what the source of the bleeding. It would seem then that only in the presence of continued improvement following aspiration without recurrence of the signs of cardiac compression should immediate suture not be advocated. (Ann. Surg., Dec. '44)

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The Effect of Intravenous Infusions in Acute Pericardial Tamponade: Evidence has recently been presented by Cooper, Stead and Warren that patients with pericardial tamponade following stab or bullet wounds of the heart may be benefited by intravenous infusions. The physiological background of the experiments, the results of which led to this conclusion, is set forth by the authors as follows:

Patients with stab wounds of the heart resulting in pericardial tamponade usually arrive at the hospital in profound shock, in coma, with cold, clammy extremities, arterial pressure too low to record and distended veins. Knowledge of the circulatory dynamics is not only of considerable theoretical interest but of practical importance in therapy as well. It is obvious that the circulation can be maintained only as long as the venous pressure exceeds the elevated intrapericardial pressure. It was believed that a consideration of the factors leading to elevation of the venous pressure might lead to a more rational basis for therapy.

The elevated venous pressure in pericardial tamponade is usually said to be produced by damming up of blood behind the obstruction to the venous inflow to the heart much as a dam causes a stream to fill up and form a lake. Such an analogy is applicable to the increase in venous pressure which may be produced in an extremity by blocking the venous outflow with a tourniquet. The retained blood fills and distends the veins of the part until the pressure within them can overcome the block. At this point the veins of the extremity contain more blood than before, this blood being obtained by compensatory vasoconstriction in other parts of the body. In this way the venous pressure in a part can be elevated practically to the level of the systolic arterial pressure. The analogy of the dammed stream is not applicable in its entirety in pericardial tamponade, because the circulation is a closed system in which the venous inflow to the heart will be decreased as a decrease in cardiac output rapidly diminishes the stream of blood entering the venous system. The venous pressure must be raised in some manner by the use of blood already in the vascular bed and not by blood being constantly fed into it from fresh sources. Blood in small amounts is obtained by vasoconstriction which forces blood from peripheral vascular beds into the larger veins. With the fall in arterial pressure less blood is contained in the arterial tree, and thus additional blood becomes available to fill and distend the venous system. Therefore, the rise in venous pressure is produced by a combination of vasoconstriction and of redistribution of blood in the vascular bed. It must be remembered that most patients with stab wounds of the heart have lost blood externally with the result that the vasoconstrictor mechanisms have already been called into play to compensate for the decrease in blood volume. Under these conditions the body is at a disadvantage in attempting to raise the venous pressure to overcome the tamponade.

Another mechanism by which venous pressure may be elevated is by increase in blood volume. Increase in blood volume is important in the elevation of the venous pressure in chronic congestive heart failure, but it does not operate in acute pericardial tamponade because the onset of the latter is almost instantaneous. The capillary pressure throughout the body is elevated so that rapid passage of fluid into the blood stream does not occur. Since maintaining adequate circulation in pericardial tamponade is dependent upon elevation

of the venous pressure, it would appear that the use of intravenous fluids to raise the venous pressure by increasing the blood volume may be beneficial.

Cooper and his co-workers produced acute pericardial tamponade in dogs by introducing saline solution through a tube into the pericardial sac. The pressure required to produce severe symptoms varied from 12 to 22 cm. A rapid intravenous infusion, with subsequent increase in blood volume, enabled the dogs to withstand an increase of pressure of from 92 to 146 per cent. In two dogs severe tamponade was produced, and intravenous saline solution caused striking improvement, even though the pericardium was closed and no fluid escaped.

The authors have administered infusions of physiologic sodium chloride solution to three patients with pericardial tamponade. In each case the arterial pressure rose and the patients became more rational. At operation the wounds in the heart and pericardium were found to have remained sealed in spite of the rise in arterial pressure.

In conclusion the authors call attention to the opinion of Blalock and Ravitch that the tamponade can frequently be relieved by aspirating blood from the pericardial cavity. Blalock and Ravitch stress the fact that in many instances the bleeding does not recur and that operation is not necessary. The results of the authors' experiments suggest that the circulatory failure in acute pericardial tamponade is counteracted by the use of intravenous infusions. This form of therapy may serve as a useful adjunct to the treatment either by aspiration or by operation. It is possible that, in certain selected patients, raising the venous pressure by increasing the blood volume will restore the circulation to a level adequate to permit the patient to survive without either aspiration or operation. (Ann. Surg., Dec. '44)

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The Relative Efficacy of Sulfonamides in Shigella Infections: Recently Hardy has reported further studies of the relative efficacy of the various sulfonamides in the treatment of bacillary dysentery. The results of these investigations confirm earlier ones reported in the Bumed News Letter of December 10, 1943.

Ten sulfonamides were used in the treatment of 1,423 patients with proved bacillary dysentery. The response to treatment was followed by comparison of daily cultures, counts being made of suspicious colonies.

The Flexner infections responded readily, the Schmitz infections a little more slowly, and the Sonne infections less satisfactorily (in two outbreaks

quite poorly). The three varieties of Shigella studied showed the same relative resistance to sulfonamides in vitro as they did in vivo.

Flexner infections in adults responded as readily with two as with four grams of absorbable sulfonamides daily. A comparable reduction of dosage in Sonne infections materially reduced the efficacy of treatment.

There were no recurrences of infection in 113 individuals who were treated for Flexner infection. These patients were held in isolation free of exposure to reinfection for two months and were tested with cultures on an average of 11.3 times per person.

Hardy grades the sulfonamides as to their relative value in the treatment of shigellosis as follows:

Superior	Sulfadiazine, sulfapyrazine, sulfasuxidine
A little less effective	Sulfamerazine, sulfamethazine
Least satisfactory of those widely tested	Sulfathiazole, sulfaguanidine
Not recommended	Sulfathaladine (less active than sulfasuxidine, a chemically related compound), sulfapyridine, sulfanilamide.

(Hardy, Nat. Inst. Health, U.S.P.H.S.)

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Comparison of Effectiveness of Quinine and Atabrine (Quinacrine) in Falciparum Malaria: The comparative activity of quinine and atabrine in the treatment of European patients infected with West African strains of Plasmodium falciparum has recently been investigated by Findlay et al. The patients were divided into two groups of 40 each. Each patient in one group received 2.0 Gm. quinine daily for 6 days. In the other group each patient received 0.8 Gm. atabrine on the first day, the total dose being 2.5 Gm. in 6 days.

While there was wide variation in the initial parasite counts in both series, in the cases treated with atabrine the average count was higher. Despite this difference in severity, there was no significant difference in the response to treatment.

The duration of fever, symptoms and parasitemia in the two groups are compared in the following table:

AVERAGE DURATION IN HOURS

Drug	Fever	Symptoms	Parasitemia
Quinine	51.0	69.0	40.2
Atabrine	54.9	63.3	43.2

Relapse, as indicated by a recrudescence of symptoms and fever and the reappearance of parasites in the blood films occurring before the patient's discharge from the hospital was seen in only one instance. This patient had been treated with quinine. Occasional return cases occurred in each group, but it is obviously not possible to distinguish between relapse and reinfection.

The authors conclude as follows: "It is still a commonly held belief that quinine is the drug of choice in the treatment of malaria, atabrine being but an inferior substitute. The results reported here show that such a view is ill-founded. It has already been demonstrated that atabrine used with heavy initial dosage can deal effectively with heavy infections by Plasmodium falciparum. The above results indicate that it can do so at least as effectively as quinine. Moreover, there is no evidence that the combination of atabrine and quinine is superior to either of these drugs used alone (Findlay, Markson and Holden, 1944).

In view of the present scarcity of quinine, there appears to be no justification for its routine use either therapeutically or as a suppressive. It should be reserved for cases exhibiting idiosyncrasy to atabrine and for emergencies such as cerebral malaria, in which the value of atabrine has yet to be demonstrated. In addition, the therapeutic administration of quinine to persons who have been receiving atabrine as a suppressive is apparently not free from the danger of inducing blackwater fever (Findlay and Stevenson, 1944)." (Report to British War Office No. 2681-44, Dec. 14, '44.)

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The Toxicity of Sodium Arsenite (Penite): Reports have been received in the Bureau that cases of arsenical dermatitis have occurred among personnel working with solutions of sodium arsenite (Penite).

A 54 per cent solution of sodium arsenite (usually diluted 1 to 40 with water at time of use) is an effective insecticide and larvicide for fly control which is used in spraying garbage dumps, latrines and bodies of the dead before burial. Precautions must be observed by personnel working with sodium arsenite to prevent inhalation of the spray mist and to avoid

contact of the skin with the solution. Individuals who have previously experienced arsenical reactions (such as dermatitis in anti-syphilitic therapy) should not be detailed to this work.

Spraying is least dangerous with a decontamination sprayer directing the spray down wind from the operators. Care should be taken that the mist does not drift to areas where other personnel will be exposed. Knapsack sprayers and hand spray guns or any equipment that is likely to expose the operator by leakage should not be used. Operators of sprayers should wear filter-type masks. Spraying should not be done in any enclosed space where the concentration of arsenite in the air may build up to toxic levels (1.5 mg. arsenic per 10 cubic meters of air).

Insofar as practicable, bodies of the dead should be prepared for burial before spraying (identification tags and personal effects removed). Bodies treated with arsenite should be marked in a conspicuous and distinctive manner as a warning. (Prev. Med. Div., BuMed - J. F. Shronts).

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Too Much Rest: The healing power of rest has been acclaimed since Hippocrates. Every doctor can recall patients who owed their recovery to the rest, physical, mental and emotional, that he brought to the pain-wracked body. Yet like all good things one can have too much of it. Those doctors who, as Cole puts it, spend their lives sending patients to bed and so establish unshakable reputations for prudence sometimes forget the shortcomings and dangers of rest as a remedy. American physicians, surgeons, obstetricians and psychiatrists lately combined to draw attention to the abuse of rest in their several branches of medicine. In traumatic surgery its limitations have been increasingly recognized - immobilize the fractured bone completely until union is sound, but actively mobilize every joint which does not need to be fixed, is becoming the accepted principle. A similar principle is beginning to be applied to general surgery. Riddoch, for instance, has protested against the long rest in bed after straightforward hernia operation or laparotomy, quoting the case of a house-surgeon who walked upstairs to her room unaided on the third day after appendicectomy, and Hill has adopted a maximum of 10 days in bed for servicemen after simple excision of a hernial sac. Powers allows his patients to get up the day after major abdominal operations, and in 100 consecutive cases saw no harm therefrom and a reduced period of convalescence. Eastman, of Baltimore, supports the views of his colleague Rotstein, that no harm is done by getting a mother up on the fourth day after delivery - in fact, that this early rising encourages involution, stimulates the lochial flow, reduces the incidence of thrombophlebitis, and leaves no higher a proportion of retroversions than the traditional ten days. Menninger has little difficulty in demonstrating that the prescribing of rest in psychiatric

and psychological disturbances is irrational, and that the restless patient needs not only rest but also the canalization of his energies into channels where they will find their legitimate and satisfying outlet.

It is perhaps in the treatment of heart disease that there is the greatest tendency toward overenthusiastic prescribing of absolute rest. In the American symposium, Harrison quoted experimental work on rats to support his clinical impression that there is seldom any need to keep patients with heart failure or coronary thrombosis in bed for the long periods usually recommended, and he emphasized the liability of bedridden patients to venous thrombosis and the development of cardiac neurosis. The risk of embolism was stressed by Dock, and Levine believes that recumbency may upset the balance between the right and left sides of the heart and thus increase the strain on the failing heart, besides increasing the total blood volume. In coronary thrombosis we must be prepared occasionally to relax our insistence on absolute rest. Until the third week of the illness absolute rest must practically always be insisted on, to ensure that only the minimum of strain is put on the myocardial infarct until healing is well established. Even in the mildest cases this is a wise rule, the only possible exception being the elderly patient. Subsequently, it may be well in some cases not to insist on the patient's staying in bed for the usual six weeks. But the patient with coronary thrombosis has often been overworking, and this may be the first adequate rest he has had for years. In the treatment of acute rheumatism the decision when to start allowing the patient to move about is often difficult to make. It is as wrong to keep a child with rheumatic fever in bed too long as to allow him to move too early. The other group of rheumatic diseases in which rest tends to be abused is arthritis. In the acute stage rest is essential, but unless we know that we can produce a cure, or at least a real improvement in the state of the joint, the patient must not be allowed to vegetate in bed. The rheumatologist is familiar enough with the patient with chronic arthritis who previously managed to contend with his crippling and lead a reasonably happy life, but entered on a slow but steady process of disintegration when he was ordered to bed. The care of the aged comes into a category by itself. Here it has long been recognized that absolute rest is seldom wise. Even when the heart is obviously failing, the old patient is often much better (and happier) sitting in a comfortable armchair than lying in bed. It is regrettable that we seldom see nowadays those large armchairs with a cushioned ledge fixed to the armpieces which used to be a constant feature of all medical wards, and in which the aged patient with a failing heart spent the greater part of his days and nights. Attention to two points will sometimes alleviate the discomforts of rest in bed. One is the use of a bedside commode rather than a bedpan; the other is massage to the legs. Every patient confined to bed, who is not suffering from an acute infection, should have daily massage to the lower limbs, unless there is a lesion of the limbs themselves. Such

massage reduces the risk of thrombus formation, helps to maintain the peripheral circulation, and insures that the muscles do not become atrophied from disuse.

In prescribing rest, then, three cardinal principles must be recognized; first, we must not overlook the close integration of mind, body and psyche; to treat one and ignore the others is to lose our chance of complete therapeutic success. Secondly, we must remember the adage about one man's meat - what is rest for one man may prove the acme of unrest for another. Thirdly, as Minot expressed it, "rest means many things to many persons." In other words, rest should not be prescribed by rule-of-thumb without considering the type of patient and the nature of the disease. (Lancet Editorial, Dec. 16, '44)

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Summary of Reports Received by the CMR: A weekly "Summary of Reports Received" is being published by the Records Section of the Committee on Medical Research of the Office of Scientific Research and Development. This Bulletin presents in abstract form selected monthly reports received by the CMR from the many civilian investigators carrying on research under contract with the OSRD. It presents also summaries of some reports received from studies being conducted by other agencies including the British and Canadian Research Councils.

From time to time items from this Bulletin which are considered to be of general interest are reproduced in the Bumed News Letter. Many of the items contained in the Bulletin are highly technical and of interest only to those doing investigative work in special fields. It would be of particular value to medical officers who are carrying on research which parallels investigative work conducted by civilian or by other military groups in this country and abroad. It would be of particular interest to medical officers who are removed by military necessity from their accustomed research and wish to keep in touch with progress in their own and related fields.

Such medical officers desiring to receive this Bulletin regularly should write to Dr. Kenneth Turner, Presbyterian Hospital, 620 West 168 Street, New York 32, New York. Inasmuch as the number of copies is limited, and hence some discretion must be exercised in acceding to requests, it is requested that applicants submit with their application a statement of the type of investigative work upon which they are engaged or in which they are interested.

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ALNAV 231

Subj: Human Plasma and Serum Albumin. 28 Dec 1944

Human plasma and serum albumin appear in the Supply Catalog, Medical Department, U.S.N., as Stock No. S1-1945 Serum Albumin (Human) 25 Gram in 100 cc. Diluent With Sterile Accessories Unit-1. Stock No. S1-3531 Plasma Normal Human Dried (500 cc. Original Plasma: Complete Injection Assembly With Diluent) Unit-1. These materials will be issued to ships Fleet Marine Force and to activities outside of continental limits of U.S. In general the quantities requested shall be estimated as follows:

Activities	Plasma (500 cc.)	Albumin (100 cc.)
APA	10 (per 100 men)	15 (per 100 men)
BB	10 "	15 "
CA	10 "	15 "
CB	10 "	15 "
CL	10 "	15 "
CV	10 "	15 "
CVE	10 "	15 "
CVL	10 "	15 "
CVB	10 "	15 "
APH	300 (initial allowance)	498 (initial allowance)
AH	500 " "	798 " "
All others outside U.S. not mentioned above	5 (per 100 men)	9 (per 100 men)
Fleet Marine Force	15 "	21 "
Extracontinental hospitals	1 (per bed)	1 (per bed)
Advance base components	1 " "	1 " "

All ships and stations should requisition the nearest storehouse or depot for sufficient amounts of these items to bring their current stock to the above required level. --SecNav. James Forrestal.

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To: All Ships and Stations. Op13-1D-mms
Serial 481813

Subj: U.S. Naval Hospital, Corvallis, Oregon - Establishment of. SO 12131
27 Dec 1944

1. The hospital facilities at the U. S. Army Camp Adair, Corvallis, Oregon, acquired from the War Department on the basis of a permit to use, are hereby established and designated as: U. S. Naval Hospital,
Corvallis, Oregon.

This is an activity of the Thirteenth Naval District.

2. Bureaus and offices concerned take necessary action.

--SecNav. James Forrestal.

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To: All Ships and Stations. Op13-1C-jc
Serial 407013

Subj: Advance Change in U. S. Navy Regulations, 1920, Article 1671(2). 23 Dec 1944

1. The following change in article 1671(2) has been approved by the President, and is promulgated in advance of a printed change. It will be included in change No. 26.

Article 1671(2) - Delete present paragraph (2) and substitute:

"(2) Members of the Nurse Corps may be transferred to the retired list for other than physical disability under the conditions stated below and the annual pay of a nurse retired under these conditions shall be three per centum of the total annual active duty pay which she was receiving at the time of retirement, multiplied by the number of complete years of service rendered prior to retirement, but not exceeding seventy-five per centum of such annual active duty pay:

"(a) An ensign in the Nurse Corps shall be recommended to the Secretary of the Navy for retirement upon reaching the age of fifty years or when she has completed twenty years of service, whichever shall occur later.

"(b) A lieutenant (junior grade) of the Nurse Corps shall be recommended to the Secretary of the Navy for retirement upon reaching the age of fifty-five years or when she has completed twenty years of service, whichever shall occur later.

"(c) A lieutenant or an officer of higher rank of the Nurse Corps shall be recommended to the Secretary of the Navy for retirement upon reaching the age of fifty-eight years or when she has completed twenty years of service, whichever shall occur later." --OpNav. W. S. Farber.

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To: All Ships and Stations. BUMED-TWS-PIL
L7-1/EN10(042)

Subj: Petrolatum, Liquid, Stock No. 1-575, Removal of from Contents of Boat Box, Stock No. 2-185, and from All Life Rafts, Life Floats and Floater Nets. 18 Dec 1944

Refs: (a) Alnav 194-44; N.D. Bul. of 15 Oct 1944, 44-1167.
(b) BuMed ltr L7-1/EN10(042), Y-ec (Form ltr No. 42), of 9 Apr 1942; N.D. Bul. Cum. Ed. 1943, 42-2097, p. 426.

1. Evidence accruing subsequent to the issue of references (a) and (b) indicates that liquid petrolatum (mineral oil) is not effective in the prevention of "immersion foot" in those who are forced to abandon ship. Therefore, reference (b) is hereby canceled and reference (a) is modified to the extent that the words "2 units stock number 1-575 and" are deleted.

2. Steps shall be taken to remove liquid petrolatum from all boat boxes, life rafts, life floats and floater nets. Liquid petrolatum thus removed shall be taken into stock by the medical department of the activity concerned.

--BuMed. Ross T. McIntire.

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To: All Ships and Stations. BUMED-O-EFB
P5-2/A9-4

Subj: Amalgam and Precious-Metal Scrap, Handling of. 20 Dec 1944

Refs: (a) BuSandA ltr L8-2/EN9(30-3)(SSD), of 25 Jul 1944.
(b) NMR&DA ltr EN9(30-3)A2-2, of 14 Oct 1944.

1. Any gold or precious metal, in form of inlays, fillings, bridges, or other appliances, taken from any patient's mouth is considered to belong to the patient and shall be given the patient. An entry to this effect shall be entered on said patient's Form H.

2. All dental activities shall collect all other amalgam, precious metal and alloy scrap derived from the practices of dentistry in the Navy and turn it over to the Medical Department property officer of the activity in which it was collected. Such collections shall be safeguarded until disposed of in accordance with next succeeding paragraphs.

3. (1) Amalgam scrap, (2) gold and platinum scrap, (3) precious metal bench sweepings, and (4) polishing residue shall be packaged separately.

4. Upon receipt of above-mentioned material the Medical Department property officer shall forward same to the supply officer of the activity for further shipment and disposal (ref. (a) and (b)).

5. This shall be done in the months of January and July of each calendar year except when a station or ship is decommissioned, at which time this material shall be turned over by the Medical Department property officer to the local supply officer for disposal. --BuMed. Ross T. McIntire.

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To: All Ships and Stations. BUMED-T L8-2/P3-3

Subj: X-Ray and Electrocardiographic Films, Conservation and Transfer of with Patients. 21 Dec 1944

Ref: (a) Alnav 82-43; N.D. Bul. Cum. Ed. 1943, 43-2022, p. 220.

1. Reference (a) emphasized the urgent need for the conservation of X-ray films. The situation in this respect continues critical and the prospects for major improvement are not encouraging.

2. To the end that films be conserved to the greatest possible degree and to insure continuity in the care of patients transferred between medical activities, addresses are directed to institute immediate administrative measures (a) to prevent duplication of expenditure of X-ray and electrocardiographic films, and (b) to transfer with the patient, clinically relevant X-ray films and electrocardiograms whenever possible.

3. When X-ray films are transferred with the patient, notation shall be made on the NavMed H-8 (Medical History Sheet) of the Health Record or other medical record, and an appropriate entry filed in the X-ray file indicating that film has been forwarded to another activity.

--BuMed. Ross T. McIntire.

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To: All Ships and Stations. BUMED-Y A3-3/EN10(104-40)

Subj: Form F, Monthly Report, Abstract of Patients - Discontinuance of. 21 Dec 1944

Ref: (a) Man. of the Med. Dept., pars. 2404, 2405 and 2406.

1. Reference directs that NavMed Form F (1940), Abstract of Patients (monthly report), shall be prepared and forwarded to the Bureau monthly and when a ship, station or hospital is placed out of commission.

2. Effective 1 January 1945, this monthly report, NavMed Form F (1940), Abstract of Patients, shall be discontinued.

3. The statistical summary on the NavMed Form F (1940), Abstract of Patients, will be incorporated in a new Monthly Morbidity Report which will supersede the present Monthly Communicable Disease Report. Instructions for the Monthly Morbidity Report will be issued within about 30 days.

4. These instructions do not affect the present procedures of submitting Nav-Med Form FA Card (Revised 1942), Individual Statistical Report of Patient.
--BuMed. Ross T. McIntire.

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To: All Ships and Stations. BUMED-RL-JRMcK
P2-5/P19-1(094)

Subj: Physical Examination Prior to Release from Active Duty or Discharge from the Naval Service. 26 Dec 1944

Ref: (a) BuMed ltr RL:JRMcK, P2-5/P19-1(094), of 30 Oct 1944; N. D. Bul. of 15 Nov 1944, 44-1263.

1. Paragraph 3 of reference (a) directed that BuMed Form Y be prepared and forwarded to the Bureau when members of the naval service are examined for release from active duty or discharged from the service, except upon the recommendation of a board of medical survey.

2. This is to advise that Forms Y will not be required in the case of recruits discharged from the service upon the recommendation of aptitude boards. Such men should, however, be given a complete and thorough physical examination when they are discharged, and the findings entered in their health records. The aptitude board reports should continue to be prepared and submitted as heretofore. --BuMed. Ross T. McIntre.

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